

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
14 April 2005 (14.04.2005)

PCT

(10) International Publication Number  
**WO 2005/032486 A3**

- (51) International Patent Classification<sup>7</sup>: A61K 48/00, C07H 21/04
- (21) International Application Number:  
PCT/US2004/032710
- (22) International Filing Date: 4 October 2004 (04.10.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/508,145 2 October 2003 (02.10.2003) US
- (71) Applicant (for all designated States except US): DUKE UNIVERSITY [US/US]; Office of Science and Technology, P.O. Box 90083, Durham, NC 27708 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): LI, Chuan-Yuan [US/US]; 300 Pebble Springs Road, Chapel Hill, NC 27514 (US). ZHANG, Xiuwu [US/CN]; 100 Dowling Bluff Drive, Morrisville, NC 27560 (US). DEWHIRST, Mark, W. [US/US]; 3610 Bran View Place, Durham, NC 27705 (US).
- (74) Agent: TAYLOR,Jr.,Aries,A.; Jenkins & Wilson, RA., Suite 1400, University Tower, 3100 Tower Boulevard, Durham, NC 27707 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, QQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:  
2 February 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2005/032486 A3

(54) Title: A NOVEL SIRNA-BASED APPROACH TO TARGET THE HIF- $\alpha$  FACTOR FOR GENE THERAPY

(57) Abstract: The presently disclosed subject matter provides vectors that encode small interfering RNAs (siRNAs) designed to down regulate the expression of hypoxia-inducible genes in a cell. Also provided are compositions and host cells based upon the vectors, as well as methods of using the vectors. The presently disclosed subject matter further provides a method of inhibiting tumor growth infecting cells in a tumor with an adenovirus vector that encodes an siRNA directed against the hypoxia-inducible factor 1 $\alpha$  (HIF-1 $\alpha$ ) gene.